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ITS BEARING UPON

STRICKER'S THEORY OF INFLAMMATION.

BY

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EXPERIMENTAL KERATITIS:

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The favourable reception that has been accorded to Prof. Stricker's theory of the pathology of inflammation as presented in the *International Encyclopædia of Surgery*, prompts me to publish an article which I prepared a year and a half ago, bearing upon the subject. It was not published before because it contained nothing essentially new. I now present it to add my experiments to those of Senftleben, Councilman, Axel Keye, Eberth and his pupils, and others. Prof. Stricker has entirely ignored the results obtained by these investigators, in spite of the fact that his own methods have been employed in obtaining specimens, and that they were exact counterparts of those described by himself. These specimens, when subjected to the influence of dyes, that stain parts before uncoloured, show changes that are diametrically opposed to his theory. The experiments are neither difficult nor complicated, and one familiar with the microscope may easily verify them, and prove to himself and to others the incompleteness of Stricker's work, and the consequent fallacy of his argument. Without further discussion or excuse the article is presented in its original form.

During the past year, at the Pathological Laboratory of the Bellevue Hospital Medical College, under the direction and the kind assistance of Prof. Welch, I have performed a number of experiments to determine the origin of pus cells, in inflammation of the cornea of cats, dogs, and frogs;[1] and the results which I invariably obtained are so much at variance with

[1] Many of my experiments were made during the spring, the most favourable time, according to Stricker; and most of them were performed upon cats, nearly grown, which he insists upon. I may say, however, that I experienced no difficulty in obtaining his pictures from the corneæ of cats of all ages, dogs, and frogs, and at all times of the year.

those claimed by some of the eminent pathologists of the present day, that I feel little hesitation in presenting them; for they can be verified by any careful observer. It is not my purpose to discuss the process of inflammation, nor will I attempt to enter the field of literature bearing upon the subject. It will suffice to state in the briefest manner, the two leading theories concerning the origin of pus cells: *first*, that of Cohnheim, who teaches the cell emigration theory, claiming that pus cells are leucocytes or wandering white blood corpuscles, and denying their origin from other sources; and *second*, that of Stricker, who adopting, with some modification, the teachings of Virchow, holds that pus cells are not emigrated cells, but that they originate from the cells of the inflamed tissue, they having returned to their embryonal condition, and from these pus cells are differentiated.

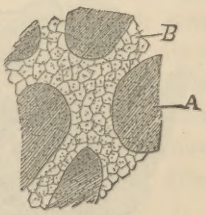
It will not be amiss to give the anatomy of the cornea before studying the changes that we shall observe in its structure. The anterior boundary of the cornea is formed by stratified epithelium; its posterior covering is a single layer of endothelium. Underneath both the epi- and endothelial coverings is a thin hyaline layer (Bowman's and Descemet's respectively) showing fine fibrillation according to some histologists. Between the last two layers the proper corneal tissue is found. It consists of fine connective tissue fibres, which run in parallel directions, forming bundles, and these in turn unite to form laminæ that run in various directions, parallel with the surface, but frequently at right angles to each other, and form the different layers of the cornea. Between the laminæ, and flattened by them, lie numerous nucleated cells—the corneal corpuscles—irregular in shape, and presenting a number of processes, which communicate with adjacent corpuscles, not necessarily between the same laminæ. Other cells —leucocytes—are often seen, and sometimes pigment cells are observed. These, with the nerve fibres, embrace about all that is to be found.[1] I have found the cat's cornea most satisfactory, because it is easy to laminate, and furnishes a large surface for experiment and observation. Irritation of the centre of the cornea was caused by various substances; the most satisfactory were silver nitrate (solid) and potassa fusa, and after intervals varying from twelve hours to a week, the cornea were removed for examination. The agents used for staining were silver nitrate and gold chloride; and subsequently the sections so stained were further stained with hæmatoxylin or carmine. The corneæ to be stained with silver nitrate, were thoroughly painted with the solid stick while the ani-

[1] Stricker thinks that the structure of the living cornea is probably homogeneous, because differences in structure appear only in post-mortem specimens and as a result of chemical or staining agents, which he thinks are due to elective affinity of certain tissue elements to these agents. Although his view conflicts with the view of the anatomy of the cornea generally accepted, it will not interfere with the question at issue, *i. e.*, the origin of pus cells.

mal was living, and ten minutes later the animal was killed; the corneæ were removed and washed in distilled water, and placed in acidulated water, where they remained usually about twenty-four hours, exposed to diffuse daylight, when they were ready for lamination or section cutting. Silver stains the intercellular substance a brownish color, and leaves the corpuscles and their processes uncoloured, so that they appear as clear spaces in the coloured field. The corneæ to be stained with gold were removed as soon as the animal was killed and washed in distilled water, and placed in fresh lemon juice, where they remained for five minutes, when they were taken out and washed again and placed in a half per cent. solution of gold chloride, in which they remained for half an hour, more or less, whence they were removed and placed in a reducing fluid, either acidulated water or, better, Pritchard's fluid (amylic alcohol 1, formic acid 1, water 100). Here they remained for twenty-four hours or more, when they were ready for lamination or cutting. Gold stains the corpuscles and their processes a purplish colour, and leaves the intercellular substance uncoloured, as clear intervals in the field—giving a picture which is the negative of that of silver. Hæmatoxylin stains the nuclei a deep blue, and the cells a more delicate tint of the same colour. Carmine stains the nucleus a delicate red or pink, and the remainder of the cell a lighter hue of the same colour.

Let us take a silver-stained cornea, 72 hours after irritation of its centre with caustic potash. A thin specimen, prepared by lamination, or cutting, is mounted in glycerine. The staining characteristic of silver is observed, and nothing peculiar is noticed until we approach the zone of the irritation; here we find the spaces corresponding to the corneal corpuscles and their processes, enlarged and occupied more or less completely by a network of fine brown mosaic tracings, claimed by Stricker to be the outlines of pus cells which have originated from corneal corpuscles. If the staining is good, cells resembling pus corpuscles can sometimes be recognized. (See Fig. 1.) If this specimen is now stained with hæmatoxylin, a beautiful picture is presented, and a most remarkable change is brought about. The silver staining is unchanged; the corneal corpuscles are now to be seen, they are of a bluish tint, and their nuclei are coloured a deeper hue; while the pus cells, with their often horseshoe-shaped nuclei (a peculiarity of the white blood-corpuscles of the cat), are stained a dark blue. We can now study the appearance, the arrangement, and the relation of parts with an intelligence impossible before this distinguishing difference was produced. We can readily map out zones, differing essentially from each other

Fig. 1.

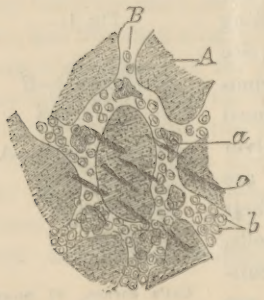


Cat's cornea, 72 hours after central irritation with caustic potash, stained with silver nitrate. *A*. Intercellular substance of a brownish colour. *B*. "Corneal spaces," occupied by delicate mosaic tracings, the outlines of pus cells.

in appearance. The first zone embraces the periphery of the cornea in which the corneal corpuscles are healthy and unchanged, and where there is an abundance of pus cells, many of which are of the ordinary appearance, with horseshoe-shaped nuclei, while others are drawn out as small rods, with elongated nuclei. In reference to the position of the pus cells, most of them occupy the spaces conjointly with the corneal corpuscles, but many of them lie in the intercellular tissue; and it is here that the rod-shaped pus cells are chiefly found. Some of the rods have one extremity in a corneal space, while the other is embedded in the intercellular substance. In passing through the interspaces of the fibrous tissue of the cornea, the leucocytes assume the size and shape of the channels they traverse thus giving rise to the rod-shaped form. The second zone lies between the corneal periphery and the central eschar; here the corneal corpuscles are unchanged, and pus cells are scanty or absent. The third and last zone embraces the central eschar and the immediately adjoining tissue.

The eschar, which has not been changed by the hæmatoyxlin, is a brownish granular mass, devoid of structure. The parts adjacent to this show the intercellular substance to be diminished, and encroached upon by enlarged corneal spaces. The corneal spaces are in most instances filled with pus cells, containing the horseshoe-shaped nuclei observed in other zones; but in those spaces not fully occupied by pus cells, the outlines of non-nucleated shrunken (dead) corneal corpuscles can be recognized. And in some instances it is possible to detect the body of a dead corneal corpuscle beneath an almost complete bridge or layer of parallel rod-shaped pus cells—the intervals between the rods are sufficient to allow a clear distinction of parts beneath. As we approach the middle zone from this point, it will be noticed that the pus cells become less numerous, and that the corneal corpuscles change at once to the normal condition, or present certain changes, that will be presently referred to. (See Fig. 2.) It is evident from a study of the above description and the accompanying cut, that the pus cells did not originate from the corneal corpuscles. That leucocytes possess a remarkable power of emigration, has been incontestably proven by Cohnheim and others; and their immigration accounts for the presence of pus cells in our specimen, in a far more satisfactory manner than can any other process. Their abundance in the peripheral zone is plainly due to emigration from adjacent conjunctival and scleral ves-

Fig. 2.



Same specimen after staining with hæmatoxylin. Both *A* and *B* the same as in Fig. 1; B, in this figure, is seen to be occupied by corneal corpuscles (*a*) and pus cells, both round (*b*) and rod-shaped (*c*).

sels—both of the latter tissues being loaded with them. The great number about the eschar is also to be explained by immigration—for here we have a denuded surface exposed to the conjunctival membrane, which furnishes a bountiful supply—the conjunctiva itself being hyperæmic or inflamed. The arrangement of the rod-shaped cells is characteristic and striking, the rods in many instances form radii with the eschar as a centre, a fact which clearly indicates that they had entered here, on their passage into the corneal tissue.

It was stated above that changes sometimes occur in the corneal capsules surrounding the eschar. This change consists in sending out delicate thread-like processes or off-shoots (regeneration spears of the Germans), the direction of which is always towards the eschar. And at some points the extremities of two spears or processes will approach each other and coalesce. Here a circumscribed enlargement is formed, from which new spears may spring. Other individual spears will terminate in bulbous enlargements, which present secondary processes. This proliferation of corneal corpuscles is plainly not pus formation. It is a regenerative process by which the living corpuscles attempt to repair the destruction caused by the caustic, by forming new corneal corpuscles.

The specimen just studied was selected because it illustrated all of the conditions which it was desired to show. It is exceptional to find one presenting all of these appearances. They will vary according to the degree of irritation, and also according to the time at which they are examined. When the cornea is moderately irritated, without an abrasion of its surface, the number of pus cells about the eschar will be small, while they will abound in the periphery of the cornea, and the regeneration spears or processes will be numerous. Whereas, if the irritation has been severe, and if there is a loss of substance, such as follows free cauterization ; the pus cells about the eschar will be abundant, and greatly in excess of those in the peripheral zones, and the regeneration spears will be slower in making their appearance. The corneal corpuscles surrounding the eschar in this instance are overcome by the pressure of leucocytes, which force their way through and crowd themselves into the adjacent tissue ; and it is only after this pressure is relieved by sloughing of the parts that the regenerative process shows itself. The regeneration spears were not observed in any specimen earlier than thirty-six hours after cauterization. They are seen to greatest advantage in gold-stained specimens. (See Figs. 3 and 4.)

As a summary, I may say, that Stricker rests his conclusions upon the appearances presented by silver-stained specimens ; that he is correct in claiming that the mosaic tracings indicate the outlines of pus cells ; but that he is wrong in his conclusions as to their origin ; and that he will continue to be mistaken so long as he confines himself to a single staining (silver). He limits his study to the eschar and its immediate vicinity,

Figs. 3 and 4.

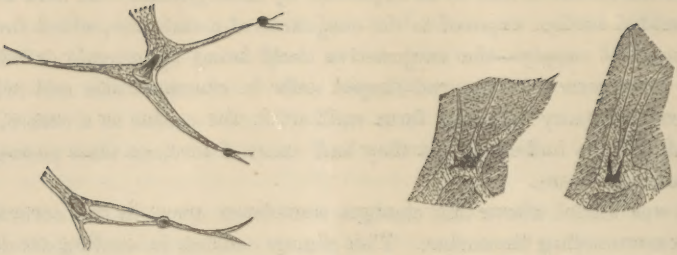


Fig. 3. Cat's cornea, 86 hours after central irritation with caustic potash, stained with gold chloride, and showing the so-called regeneration spears.

Fig. 4. Cat's cornea, 86 hours after central irritation with caustic potash, stained with silver, showing regeneration *spears*.

All of these specimens were taken from the zone surrounding the eschar.

because silver-stained specimens show changes in no other locality. We claim to have established the immigration theory; because the pus cells are similar in appearance to the white blood-corpuscles (both have horse-shoe-shaped nuclei in cats); they can be traced from the corneal periphery to the point of irritation; and having also gained access to the corneal tissue through the eschar, they are most abundant immediately around this centre, where we can still recognize dead, but intact, corneal corpuscles. The corneal corpuscles show signs of proliferation, some time after the cell immigration has set in; and this proliferation gives rise, not to pus cells, but to new corneal corpuscles, and they are strictly limited to the zone surrounding the dead corneal corpuscles; whereas leucocytes, or pus cells, in abundance, can be found in various parts of the cornea, at a distance from this point.

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